The Relax Study - REduction of the autonomic stress response with AnXiolytics
A double blind randomized clinical trial of alprazolam vs. placebo on social stress-induced hyperthermia response in healthy men

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Study ObjectiveTo determine whether alprazolam, a registered anxiolytic non-selective benzodiazepine, can reduce the autonomic temperature increase induced with social stress in healthy men. Secondary objectives are to determine whether alprazolam...

Ethical review	Not approved
Status	Will not start
Health condition type	Anxiety disorders and symptoms
Study type	Interventional

Summary

ID

NL-OMON31720

Source
ToetsingOnline

Brief title
RELAX study

Condition

- Anxiety disorders and symptoms

Synonym
anxiety disorders, impaired stress responses

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: alprazolam, anxiolytics, stress, temperature

Outcome measures

Primary outcome

7. Outcome measures

7.1 Primary outcome measure

The primary outcome measure is the reduction of the stress-induced hyperthermia

response during/after the TSST.

Secondary outcome

7. Outcome measures

7.2 Secondary outcome measures

The Secondary outcome measures are

- Blood pressure during the TSST

- Correlation of saliva cortisol levels with the stress-induced hyperthermia

response

- Correlation of the stress-induced hyperthermia response and stress-inuduced

blood pressure response with a set of anxiety/stress questionnaires

Study description

Background summary

Acute stress elicits an autonomic stress response, causing body temperature to rise in all organisms (stress-induced hyperthermia, SIH) . This autonomic stress response also causes the blood pressure and heart rate to increase, and plays an important part in the manifestation of anxiety disorders, when it is activated inappropriately. Extensive animal research has shown that this SIH response can be robustly blocked with a wide range of anxiolytic drugs. Furthermore, the SIH response has excellent translational properties for anxiety research, because the procedure and parameters are more or less identical in animals as well as humans. So far, very little structural research on the autonomic stress response in humans has been carried out. Therefore, the RELAX study aims to reduce the SIH response in healthy men exposed to social stress with one dose of the registered anxiolytic drug alprazolam. In addition, we aim to reduce the stress-induced increase in blood pressure using an automatic blood pressure monitor. Furthermore, we aim to correlate the stress-induced hyperthermia response with the stress-induced cortisol response by measuring saliva cortisol during the stress test. Moreover, we aim to correlate the autonomic stress-induced temperature response to subjective perceived anxiety levels in humans by using a set of anxiety/stress questionnaires. The possibility to screen for stress and anxiety using temperature measurements could be of great clinical value. Also, this experiment would also provide evidence for a complete translational anxiety model which can be identically carried out in animals as well as humans, facilitating progress in anxiety research.

Study objective

Study Objective
To determine whether alprazolam, a registered anxiolytic non-selective benzodiazepine, can reduce the autonomic temperature increase induced with social stress in healthy men. Secondary objectives are to determine whether alprazolam can reduce the autonomic blood pressure increase, wether the SIH response correlates with the stress-induced cortisol response (positive control) and whether the SIH response correlates with subjective perceived stress/anxiety levels.

Study design

Study Design
This is a small placebo-controlled, double-blind, randomized controlled trial of alprazolam versus placebo in 24 adult male volunteers exposed to social stress via the validated Trier Social Stress Test. Body temperature and blood pressure will be measured throughout stress exposure using an ingested telemetry pill and a automatic blood pressure monitor, and subjects will donate saliva samples before, during and after the Trier Social Stress Test. Also,

volunteers complete anxiety/stress questionnaires twice.

Intervention

6. Interventions
6.1 Telemetry pill
All participants receive and ingest a telemetry pill (Vitalsense Minimitter, size 2.3 x 0.87 cm) on the day of the TSST, at least 2 hours before commencing the TSST. Immediately after taking the pill, temperature data will be checked to establish a good functioning of the telemetry pill. The pill will be present until it leaves the alimentary tract after an average passage time of 1 day which is sufficient for this study. The pill will leave the body without any known hazard or discomfort. For details about the system and MDD/FDA approvals, we refer to Appendix B.

6.2 Blood pressure monitor
All volunteers will be equipped with an automatic blood pressure monitor at least 2 hours before commencing the TSST which will measure the blood pressure at regular intervals.

6.3 Alprazolam group (index treatment)
Participants randomized to the alprazolam group receive a single oral dose of alprazolam (1.0 mg) 1 hour before commencing the TSST.

6.4 Placebo control group
Participants randomized to the control group receive a single oral dose of placebo
1 hour before commencing the TSST.

Trial medication (alprazolam or placebo) is handed out by the attending investigator.
Volunteers and investigators are blinded for treatment allocation.

6.5 Stress procedure
6.5.1 General
All stress tests will be taken in the morning (8:00 until 14:00) since body temperature and cortisol levels are subject to circadian rhythmicity. In addition, we will make sure that volunteers are awake at least one hour before starting by phone calls since a shorter period could influence stress behaviour. Also, no heavy physical exercise should be exerted or large meals should be taken on the morning before the stress procedure.

6.5.2 The Trier Social Stress Test
The Trier Social Stress Test is a procedure which was developed at the University of Trier for induction of moderate psychosocial stress under laboratory conditions (Kirschbaum, Pirke et al. 1993). In numerous studies in

Trier and other laboratories, the TSST has proven to elicit significant changes in cardiovascular parameters, different endocrine axes as well as subjective stress ratings. To ensure that the results obtained in response to this challenge test remain comparable over time, it is necessary to standardize its execution, so that every volunteer is challenged similarly during confrontation with the Trier Social Stress Test. For a precise protocol of the Trier Social Stress Test we refer to Appendix A of the study protocol (p 14), where all details are written down. These procedures are standardized and validated.

Study burden and risks

Volunteers have no direct benefit of participation. No risks are associated with the ingestable telemetry pill and alprazolam. The Trier Social Stress Test is a standardized form of social stress with no extra burden for an academic student.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

healthy male students over 18

Exclusion criteria

Exclusion criteria are: female gender, smoking more than 5 cigarettes a day, any psychiatric disorder, any significant medical condition including any gastrointestinal condition that would lead to a contraindication for the telemetric pill, participation in current psychological or psychopharmacological treatment, use of any medication which might influence autonomic response, including psychotropics, beta blockers, ACE inhibitors and any hormonal treatment. Acute exclusion criteria are: any acute illness, fever, having a severe cold, recent physical exertion within the last 2 hours, large meals.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	24
Type:	Anticipated

Medical products/devices used

Generic name:	ingestable radiotelemetry pill / automatic blood pressure monitor

Registration:	Yes - CE intended use

Ethics review

Not approved

Date:	24-06-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL21089.041.08